

WE CLAIM:

1. A heterologous fusion protein comprising a hyperglycosylated G-CSF analog fused to a polypeptide selected from the group consisting of
 - d) human albumin;
 - e) human albumin analogs; and
 - f) fragments of human albumin.
2. The heterologous fusion protein of claim 1, wherein the hyperglycosylated G-CSF analog is fused to the polypeptide via a peptide linker.
3. The heterologous fusion protein of the Claim 2 wherein the peptide linker is selected from the group consisting of:
 - c) a glycine rich peptide;
 - d) a peptide having the sequence [Gly-Gly-Gly-Gly-Ser]_n where n is 1, 2, 3, 4, or 5; and
 - e) a peptide having the sequence [Gly-Gly-Gly-Gly-Ser]₃.
4. The heterologous fusion protein of Claims 1, 2, or 3 wherein the hyperglycosylated G-CSF analog comprises the amino acid sequence of the formula I: [SEQ ID NO: 1]

1	5	10	15												
Thr	Pro	Leu	Gly	Pro	Ala	Ser	Ser	Leu	Pro	Gln	Ser	Phe	Leu	Leu	Lys
	20					25							30		
Xaa	Leu	Glu	Gln	Val	Arg	Lys	Ile	Gln	Gly	Asp	Gly	Ala	Ala	Leu	Gln
	35					40							45		
Glu	Lys	Leu	Cys	Xaa	Xaa	Xaa	Lys	Leu	Cys	His	Pro	Glu	Glu	Leu	Val
	50					55						60			
Leu	Leu	Gly	His	Ser	Leu	Gly	Ile	Xaa							
	65					70				75			80		
Xaa	Xaa	Xaa	Xaa	Gln	Leu	Ala	Gly	Cys	Leu	Ser	Gln	Leu	His	Ser	
													85	90	95
Gly	Leu	Phe	Leu	Tyr	Gln	Gly	Leu	Leu	Gln	Ala	Leu	Xaa	Xaa	Xaa	Ser
	100					105							110		
Xaa	Glu	Leu	Gly	Pro	Thr	Leu	Asp	Thr	Leu	Gln	Leu	Asp	Val	Ala	Asp
	115					120							125		
Phe	Ala	Thr	Thr	Ile	Trp	Gln	Gln	Met	Glu	Glu	Leu	Gly	Met	Ala	Pro

- 58 -

130	135	140													
Ala	Leu	Gln	Pro	Xaa	Xaa	Xaa	Ala	Met	Pro	Ala	Phe	Xaa	Xaa	Xaa	Phe
145				150					155						160
Gln	Arg	Arg	Ala	Gly	Gly	Val	Leu	Val	Ala	Ser	His	Leu	Aln	Ser	Phe
				165				170							
Leu	Glu	Val	Ser	Tyr	Arg	Val	Leu	Arg	His	Leu	Ala	Gln	Pro		(I)

wherein:

Xaa at position 17 is Cys, Ala, Leu, Ser, or Glu;
Xaa at position 37 is Ala or Asn;
Xaa at position 38 is Thr, or any other amino acid except Pro;
Xaa at position 39 is Tyr, Thr, or Ser;
Xaa at position 57 is Pro or Val;
Xaa at position 58 is Trp or Asn;
Xaa at position 59 is Ala or any other amino acid except Pro;
Xaa at position 60 is Pro, Thr, Asn, or Ser,
Xaa at position 61 is Leu, or any other amino acid except Pro;
Xaa at position 62 is Ser or Thr;
Xaa at position 63 is Ser or Asn;
Xaa at position 64 is Cys or any other amino acid except Pro;
Xaa at position 65 is Pro, Ser, or Thr;
Xaa at position 66 is Ser or Thr;
Xaa at position 67 is Gln or Asn;
Xaa at position 68 is Ala or any other amino acid except Pro;
Xaa at position 69 is Leu, Thr, or Ser
Xaa at position 93 is Glu or Asn
Xaa at position 94 is Gly or any other amino acid except Pro;
Xaa at position 95 is Ile, Asn, Ser, or Thr;
Xaa at position 97 is Pro, Ser, Thr, or Asn;
Xaa at position 133 is Thr or Asn;
Xaa at position 134 is Gln or any other amino acid except Pro;
Xaa at position 135 is Gly, Ser, or Thr
Xaa at position 141 is Ala or Asn;
Xaa at position 142 is Ser or any other amino acid except Pro; and
Xaa at position 143 is Ala, Ser, or Thr;

and wherein:

Xaa at positions 37, 38, and 39 constitute region 1;
Xaa at positions 58, 59, and 60 constitute region 2;
Xaa at positions 59, 60, and 61 constitute region 3;

- 59 -

Xaa at positions 60, 61, and 62 constitute region 4;
Xaa at positions 61, 62, and 63 constitute region 5;
Xaa at positions 62, 63, and 64 constitute region 6;
Xaa at positions 63, 64, and 65 constitute region 7;
Xaa at positions 64, 65, and 66 constitute region 8;
Xaa at positions 67, 68, and 69 constitute region 9;
Xaa at positions 93, 94, and 95 constitute region 10;
Xaa at positions 94, 95, and Ser at position 96
constitute region 11;
Xaa at positions 95, and 97, and Ser at position 96
constitute region 12;
Xaa at positions 133, 134, and 135 constitute
region 13;
Xaa at positions 141, 142, and 143 constitute
region 14;

and provided that at least one of regions 1 through 14
comprises the sequence Asn Xaa1 Xaa2 wherein Xaa1 is any
amino acid except Pro and Xaa2 is Ser or Thr.

5. The heterologous fusion protein of Claim 4 wherein any
two regions of regions 1 through 14 comprise the sequence
Asn Xaa1 Xaa2 wherein Xaa1 is any amino acid except Pro and
Xaa2 is Ser or Thr.

6. The heterologous fusion protein of Claim 4 wherein any
three regions of regions 1 through 14 comprise the sequence
Asn Xaa1 Xaa2 wherein Xaa1 is any amino acid except Pro and
Xaa2 is Ser or Thr.

7. The heterologous fusion protein of Claim 4 wherein any
four regions of regions 1 through 14 comprise the sequence
Asn Xaa1 Xaa2 wherein Xaa1 is any amino acid except Pro and
Xaa2 is Ser or Thr.

- 60 -

8. The heterologous fusion protein of Claim 4 wherein the hyperglycosylated G-CSF analog is selected from the group consisting of:

- a) G-CSF [A37N, Y39T]
- b) G-CSF [P57V, W58N, P60T]
- c) G-CSF [P60N, S62T]
- d) G-CSF [S63N, P65T]
- e) G-CSF [Q67N, L69T]
- f) G-CSF [E93N, I95T]
- g) G-CSF [T133N, G135T]
- h) G-CSF [A141N, A143T]
- i) G-CSF [A37N, Y39T, P57V, W58N, P60T]
- j) G-CSF [A37N, Y39T, P60N, S62T]
- k) G-CSF [A37N, Y39T, S63N, P65T]
- l) G-CSF [A37N, Y39T, Q67N, L69T]
- m) G-CSF [A37N, Y39T, E93N, I95T]
- n) G-CSF [A37N, Y39T, T133N, G135T]
- o) G-CSF [A37N, Y39T, A141N, A143T]
 - p) G-CSF [A37N, Y39T, P57V, W58N, P60T, S63N, P65T]
- q) G-CSF [A37N, Y39T, P57V, W58N, P60T, Q67N, L69T]
- r) G-CSF [A37N, Y39T, S63N, P65T, E93N, I95T].

9. The heterologous fusion protein of claim 8, wherein the hyperglycosylated G-CSF analog is G-CSF [A37N, Y39T, P57V, W58N, P60T, Q67N, L69T].

10. The heterologous fusion protein of claim 8, wherein the hyperglycosylated G-CSF analog is G-CSF [A37N, Y39T, S63N, P65T, E93N, I95T].

11. A heterologous fusion protein which is the product of the expression in a host cell of an exogenous DNA sequence which comprises a DNA sequence encoding a heterologous fusion protein of any one of Claims 1 through 11.

12. An isolated nucleic acid sequence, comprising a

- 61 -

polynucleotide encoding a heterologous fusion protein of any one of Claims 1 through 11.

13. An isolated nucleic acid sequence, comprising a polynucleotide which comprises a DNA sequence selected from the group consisting of:

a) SEQ ID NO:2

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC

GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CGC CGT CGC GAG GTC

GAG AAG CTG TGT GCC ACC TAC AAG CTG TGC CAC CCC GAG GAG CTG GTG CTC TTC GAC ACA CGG TGG ATG TTC GAC ACG GTG GGG CTC CTC GAC CAC

CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AGC TGC GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TCG ACG

CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC GGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG

GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG

CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG

TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA

GCC CTG CAG CCC AAC CAG ACC GCC ATG CCG GCC TTC GCC TCT GCT TTC CGG GAC GTC GGG TTG GTC TGG CGG TAC GGC CGG AAG CGG AGA CGA AAG

CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC GTC CGC GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG

CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

b) SEQ ID NO:3

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC

GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CGC CGT CGC GAG GTC

GAG AAG CTG TGT GCC ACC TAC AAG CTG TGC CAC CCC GAG GAG CTG GTG CTC TTC GAC ACA CGG TGG ATG TTC GAC ACG GTG GGG CTC CTC GAC CAC

CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AGC TGC GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TCG ACG

CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC

- 62 -

GGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG
 GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
 CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG
 CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
 GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
 TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
 AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT CTT GAC CCT TAC CGG GGA
 GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC AAC TCT ACC TTC
 CGG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG TTG AGA TGG AAG
 CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
 GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
 CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
 GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

c) SEQ ID NO:4

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
 TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC
 GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
 CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CGG CGT CGC GAG GTC
 GAG AAG CTG TGT AAC ACC AAG CTG TGC CAC CCC GAG GAG CTG GTG
 CTC TTC GAC ACA TTG TGG TGG TTC GAC ACG GTG GGG CTC CTC GAC CAC
 CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AGC TGC
 GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TCG ACG
 CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
 GGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG
 GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
 CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG
 CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
 GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
 TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
 AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT CTT GAC CCT TAC CGG GGA
 GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
 CGG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG
 CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
 GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
 CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
 GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

d) SEQ ID NO:5

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
 TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC

- 63 -

GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC
GAG AAG CTG TGT GCC ACC TAC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA CGG TGG ATG TTC GAC ACG GTG GGG CTC CTC GAC CAC
CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT AAC ACT AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA TTG GAC TCC TCG ACG
CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG GTC CGG GAC GTC CGT ACG AAC TCG GTT GAG GTA TCG
GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG
CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA
GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CCG GAC GTC CGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG
CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

e) SEQ ID NO:6

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC
GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC
GAG AAG CTG TGT GCC ACC TAC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA CGG TGG ATG TTC GAC ACG GTG GGG CTC CTC GAC CAC
CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AAT TGC
GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TTA ACG
ACC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
TGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG
GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG
CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA
GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CCG GAC GTC CGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG

- 64 -

CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG

CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

f) SEQ ID NO:7

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC

GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC

GAG AAG CTG TGT GCC ACC TAC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA CGG TGG ATG TTC GAC ACG GTG GGG CTC CTC GAC CAC

CTG CTC GGA CAC TCT CTG GGC ATC GTT AAC GCT ACC CTG AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG CAA TTG CGA TGG GAC TCG TCG ACG

CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG

GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG

CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG

TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT CTT GAC CCT TAC CGG GGA

GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CCG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG

CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG

CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

g) SEQ ID NO:8

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC

GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC

GAG AAG CTG TGT GCC ACC TAC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA CGG TGG ATG TTC GAC ACG GTG GGG CTC CTC GAC CAC

CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TCG ACG

CCC AGC AAC GCC ACC CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG TTG CGG TGG GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG

GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC

- 65 -

CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG
CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA
GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CCG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG
CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

h) SEQ ID NO:9

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC
GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CCG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC
GAG AAG CTG TGT GCC ACC TAC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA CGG TGG ATG TTC GAC ACG GTG GGG CTC CTC GAC CAC
CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TCG ACG
CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG
GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG AAC GGG ACC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC TTG CCC TGG AGG
CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA
GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CCG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG
CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

i) SEQ ID NO:10

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC
GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CCG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC

- 66 -

GAG AAG CTG TGT AAC ACC ACC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA TTG TGG TTC GAC ACG GTG GGG CTC CTC GAC CAC
CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TCG ACG
CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG
GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG
CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA
GCC CTG CAG CCC AAC CAG ACC GCC ATG CCG GCC TTC GCC TCT GCT TTC
CCG GAC GTC GGG TTG GTC TGG CGG TAC GGC CGG AAG CGG AGA CGA AAG
CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG
j) SEQ ID NO:11
ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC
GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC
GAG AAG CTG TGT AAC ACC ACC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA TTG TGG TGG TTC GAC ACG GTG GGG CTC CTC GAC CAC
CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TCG ACG
CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG
GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG
CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA
GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC AAC TCT ACC TTC
CCG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG TTG AGA TGG AAG
CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG

- 67 -

CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

k) SEQ ID NO:12

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC

GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC

GAG AAG CTG TGT AAC ACC ACC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA TTG TGG TGG TTC GAC ACG GTG GGG CTC CTC GAC CAC

CTG CTC GGA CAC TCT CTG GGC ATC GTT AAC GCT ACC CTG AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG CAA TTG CGA TGG GAC TCG TCG ACG

CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG

GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG

CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG

TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA

GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CGG GAC GTC CGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG

CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG

CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

1) SEQ ID NO:13

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC

GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC

GAG AAG CTG TGT AAC ACC ACC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA TTG TGG TGG TTC GAC ACG GTG GGG CTC CTC GAC CAC

CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TCG ACG

CCC AGC AAC GCC ACC CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG TTG CGG TGG GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG

GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG

- 68 -

CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT CTT GAC CCT TAC CGG GGA
GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CGG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG
CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

m) SEQ ID NO:14

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC
GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC
GAG AAG CTG TGT AAC ACC ACC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA TTG TGG TGG TTC GAC ACG GTG GGG CTC CTC GAC CAC
CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TCG ACG
CCC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG
GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG
AAC GGT ACC GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
TTG CCA TGG CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA

GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CGG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG
CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG

n) SEQ ID NO:15

ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC
GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CCG CGT CGC GAG GTC
GAG AAG CTG TGT AAC ACC ACC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA TTG TGG TGG TTC GAC ACG GTG GGG CTC CTC GAC CAC

- 69 -

CTG CTC GGA CAC TCT CTG GGC ATC GTT AAC GCT ACC CTG AGC AGC TGC
GAC GAG CCT GTG ACA GAC CCG TAG CAA TTG CGA TGG GAC TCG TCG ACG
CCC AGC AAC GCC ACC CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
GGG TCG TTG CGG TGG GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG
GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG GAA GGG ATC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC CTT CCC TAG AGG
CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA
GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CCG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG
CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG
o) SEQ ID NO:16
ACC CCC CTG GGC CCT GCC AGC TCC CTG CCC CAG AGC TTC CTG CTC AAG
TGG GGG GAC CCG GGA CGG TCG AGG GAC GGG GTC TCG AAG GAC GAG TTC
GCC TTA GAG CAA GTG AGG AAG ATC CAG GGC GAT GGC GCA GCG CTC CAG
CGG AAT CTC GTT CAC TCC TTC TAG GTC CCG CTA CGG CGT CGC GAG GTC
GAG AAG CTG TGT AAC ACC ACC AAG CTG TGC CAC CCC GAG GAG CTG GTG
CTC TTC GAC ACA TTG TGG TGG TTC GAC ACG GTG GGG CTC CTC GAC CAC
CTG CTC GGA CAC TCT CTG GGC ATC CCC TGG GCT CCC CTG AGC AAT TGC
GAC GAG CCT GTG ACA GAC CCG TAG GGG ACC CGA GGG GAC TCG TTA ACG
ACC AGC CAG GCC CTG CAG CTG GCA GGC TGC TTG AGC CAA CTC CAT AGC
TGG TCG GTC CGG GAC GTC GAC CGT CCG ACG AAC TCG GTT GAG GTA TCG
GGC CTT TTC CTC TAC CAG GGG CTC CTG CAG GCC CTG AAC GGG ACC TCC
CCG GAA AAG GAG ATG GTC CCC GAG GAC GTC CGG GAC TTG CCC TGG AGG
CCC GAG TTG GGT CCC ACC TTG GAC ACA CTG CAG CTG GAC GTC GCC GAC
GGG CTC AAC CCA GGG TGG AAC CTG TGT GAC GTC GAC CTG CAG CGG CTG
TTT GCC ACC ACC ATC TGG CAG CAG ATG GAA GAA CTG GGA ATG GCC CCT
AAA CGG TGG TGG TAG ACC GTC GTC TAC CTT GAC CCT TAC CGG GGA
GCC CTG CAG CCC ACC CAG GGT GCC ATG CCG GCC TTC GCC TCT GCT TTC
CCG GAC GTC GGG TGG GTC CCA CGG TAC GGC CGG AAG CGG AGA CGA AAG
CAG CGC CGG GCA GGA GGG GTC CTG GTT GCC TCC CAT CTG CAG AGC TTC
GTC GCG GCC CGT CCT CCC CAG GAC CAA CGG AGG GTA GAC GTC TCG AAG
CTG GAG GTG TCG TAC CGC GTC TTA AGG CAC CTT GCC CAG CCC
GAC CTC CAC AGC ATG GCG CAG AAT TCC GTG GAA CGG GTC GGG,

- 70 -

fused to a DNA encoding a protein selected from the group consisting of:

- a) human albumin,
- b) human albumin analog; and
- c) fragments of human albumin.

14. The heterologous fusion protein of any one of Claims 1 through 11 wherein the polypeptide is human albumin.

15. The heterologous fusion protein of Claim 12, wherein the second polypeptide has the sequence of SEQ ID NO: 35.

16. The heterologous fusion protein of any one of Claims 1 through 11 wherein the second polypeptide is an N-terminal fragment of albumin.

17. A method for increasing neutrophil levels in a mammal comprising the administration of a therapeutically effective amount of the heterologous fusion protein of any one of Claims 1 through 11, 14 and 15.

18. The use of the heterologous fusion protein as claimed in any one of Claims 1 through 11, 14 and 15 for the manufacture of a medicament for the treatment of patients with insufficient circulating neutrophil levels.

19. Use of a heterologous fusion protein of any one of Claims 1 through 11, 14, and 15 as a medicament.

20. Use of a heterologous fusion protein of any one of Claims 1 through 11, 14, and 15 for the treatment of patients with insufficient circulating neutrophil levels.

21. A pharmaceutical formulation adapted for the treatment of patients with insufficient neutrophil levels comprising a

- 71 -

heterologous fusion protein of any one of Claims 1 through 11, 14, and 15.

22. A heterologous fusion protein comprising a hyperglycosylated G-CSF analog fused to a polypeptide selected from the group consisting of

- a) the Fc portion of an immunoglobulin;
- b) an analog of the Fc portion of an immunoglobulin;
and
- c) fragments of the Fc portion of an immunoglobulin.

23. The heterologous fusion protein of Claim 22, wherein the hyperglycosylated G-CSF analog is fused to the polypeptide via a peptide linker.

24. The heterologous fusion protein of the Claim 23 wherein the peptide linker is selected from the group consisting of:

- a) a glycine rich peptide;
- b) a peptide having the sequence [Gly-Gly-Gly-Gly-Ser]_n where n is 1, 2, 3, 4, or 5; and
- c) a peptide having the sequence [Gly-Gly-Gly-Gly-Ser]₃.

23. The heterologous fusion protein of Claims 22, 23 or 24, wherein the hyperglycosylated G-CSF analog comprises the amino acid sequence of the formula I: [SEQ ID NO: 1]

1	5	10	15
Thr Pro Leu Gly Pro Ala Ser Ser	Leu Pro Gln Ser Phe Leu Leu Lys		
20	25		30
Xaa Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln			
35	40		45
Glu Lys Leu Cys Xaa Xaa Xaa Lys Leu Cys His Pro Glu Glu Leu Val			
50	55		60
Leu Leu Gly His Ser Leu Gly Ile Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa			
65	70		75
Xaa Xaa Xaa Xaa Xaa Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser			
85	90		95
Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Xaa Xaa Xaa Ser			
100	105		110
Xaa Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp			
115	120		125
Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro			
130	135		140
Ala Leu Gln Pro Xaa Xaa Xaa Ala Met Pro Ala Phe Xaa Xaa Xaa Phe			
145	150		155
			160

- 72 -

Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Aln Ser Phe
165 170
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro (I)

wherein:

Xaa at position 17 is Cys, Ala, Leu, Ser, or Glu;
Xaa at position 37 is Ala or Asn;
Xaa at position 38 is Thr, or any other amino acid except Pro;
Xaa at position 39 is Tyr, Thr, or Ser;
Xaa at position 57 is Pro or Val;
Xaa at position 58 is Trp or Asn;
Xaa at position 59 is Ala or any other amino acid except Pro;
Xaa at position 60 is Pro, Thr, Asn, or Ser,
Xaa at position 61 is Leu, or any other amino acid except Pro;
Xaa at position 62 is Ser or Thr;
Xaa at position 63 is Ser or Asn;
Xaa at position 64 is Cys or any other amino acid except Pro;
Xaa at position 65 is Pro, Ser, or Thr;
Xaa at position 66 is Ser or Thr;
Xaa at position 67 is Gln or Asn;
Xaa at position 68 is Ala or any other amino acid except Pro;
Xaa at position 69 is Leu, Thr, or Ser
Xaa at position 93 is Glu or Asn
Xaa at position 94 is Gly or any other amino acid except Pro;
Xaa at position 95 is Ile, Asn, Ser, or Thr;
Xaa at position 97 is Pro, Ser, Thr, or Asn;
Xaa at position 133 is Thr or Asn;
Xaa at position 134 is Gln or any other amino acid except Pro;
Xaa at position 135 is Gly, Ser, or Thr
Xaa at position 141 is Ala or Asn;
Xaa at position 142 is Ser or any other amino acid except Pro; and
Xaa at position 143 is Ala, Ser, or Thr;

and wherein:

Xaa at positions 37, 38, and 39 constitute region 1;
Xaa at positions 58, 59, and 60 constitute region 2;
Xaa at positions 59, 60, and 61 constitute region 3;
Xaa at positions 60, 61, and 62 constitute region 4;

- 73 -

Xaa at positions 61, 62, and 63 constitute region 5;
Xaa at positions 62, 63, and 64 constitute region 6;
Xaa at positions 63, 64, and 65 constitute region 7;
Xaa at positions 64, 65, and 66 constitute region 8;
Xaa at positions 67, 68, and 69 constitute region 9;
Xaa at positions 93, 94, and 95 constitute region 10;
Xaa at positions 94, 95, and Ser at position 96
constitute region 11;
Xaa at positions 95, and 97, and Ser at position 96
constitute region 12;
Xaa at positions 133, 134, and 135 constitute
region 13;
Xaa at positions 141, 142, and 143 constitute
region 14;

and provided that at least one of regions 1 through 14
comprises the sequence Asn Xaa1 Xaa2 wherein Xaa1 is any
amino acid except Pro and Xaa2 is Ser or Thr.

26. The heterologous fusion protein of Claim 25 wherein any
two regions of regions 1 through 14 comprise the sequence
Asn Xaa1 Xaa2 wherein Xaa1 is any amino acid except Pro and
Xaa2 is Ser or Thr.

27. The heterologous fusion protein of Claim 25 wherein any
three regions of regions 1 through 14 comprise the sequence
Asn Xaa1 Xaa2 wherein Xaa1 is any amino acid except Pro and
Xaa2 is Ser or Thr.

28. The heterologous fusion protein of Claim 25 wherein any
four regions of regions 1 through 14 comprise the sequence
Asn Xaa1 Xaa2 wherein Xaa1 is any amino acid except Pro and
Xaa2 is Ser or Thr.

- 74 -

29. The heterologous fusion protein of Claim 25 wherein the hyperglycosylated G-CSF analog is selected from the group consisting of:

- a) G-CSF [A37N, Y39T]
- b) G-CSF [P57V, W58N, P60T]
- c) G-CSF [P60N, S62T]
- d) G-CSF [S63N, P65T]
- e) G-CSF [Q67N, L69T]
- f) G-CSF [E93N, I95T]
- g) G-CSF [T133N, G135T]
- h) G-CSF [A141N, A143T]
- i) G-CSF [A37N, Y39T, P57V, W58N, P60T]
- j) G-CSF [A37N, Y39T, P60N, S62T]
- k) G-CSF [A37N, Y39T, S63N, P65T]
- l) G-CSF [A37N, Y39T, Q67N, L69T]
- m) G-CSF [A37N, Y39T, E93N, I95T]
- n) G-CSF [A37N, Y39T, T133N, G135T]
- o) G-CSF [A37N, Y39T, A141N, A143T]
- p) G-CSF [A37N, Y39T, P57V, W58N, P60T, S63N, P65T]
- q) G-CSF [A37N, Y39T, P57V, W58N, P60T, Q67N, L69T]
- r) G-CSF [A37N, Y39T, S63N, P65T, E93N, I95T] .

30. The heterologous fusion protein of Claim 29 wherein the hyperglycosylated G-CSF analog is G-CSF [A37N, Y39T, P57V, W58N, P60T, Q67N, L69T] .

31. The heterologous fusion protein of Claim 29 wherein the hyperglycosylated G-CSF analog is G-CSF [A37N, Y39T, S63N, P65T, E93N, I95T] .

32. The heterologous fusion protein of any one of Claims 22 through 31 wherein the second polypeptide is the Fc portion of an Ig selected from the group consisting of: IgG1, IgG2, IgG3, IgG4, IgE, IgA, IgD, or IgM.

- 75 -

33. The heterologous fusion protein of any one of Claims 22 through 32 wherein the second polypeptide is the Fc portion of an Ig selected from the group consisting of: IgG1, IgG2, IgG3, and IgG4.

34. The heterologous fusion protein of Claim 33 wherein the second polypeptide is the Fc portion of an IgG1 immunoglobulin.

35. The heterologous fusion protein of Claim 33 wherein the second polypeptide is the Fc portion of an IgG4 immunoglobulin.

36. The heterologous fusion protein of Claims 22 through 35 wherein the IgG is human.

37. The heterologous fusion protein of any one of Claims 22 through 36 wherein the Fc portion comprises the hinge, CH2, and CH3 domains.

38. The heterologous fusion protein of Claim 34 wherein the polypeptide has the sequence of SEQ ID NO: 33.

39. The heterologous fusion protein of Claim 34, wherein the polypeptide has the following nucleic acid sequence:

tccaccaaggcccattcggtctcccgtagcgccctgctccaggagcaccccgagac
acagccgcctggctgcctgg
tcaaggactactcccgAACCCGGTgacgggtgtcgtaactcaggcgccctgaccagcg
gcgtgcacacccctccggctgtc
ctacagtccctcaggactactccctcagcagcgtggtgaccgtgcctccagcagcttgc
ggcacagaagacccatcacacccgtcaac
gtagatcacaagcccagcaacaccaagggtggacaagagagttgagtccaaatatggtccc
ccatgccaccctgcccagca
cctgagttccctgggggaccatcagtctccctgttccccccaaaacccaaaggacactctc
atgatctcccgaccctgaggcac
gtgcgtgggtggacgtgagccaggaagaccccgaggtccagttcaactggtacgtgga
tggcgtggagggtgcataatgcca
agacaaaaggccggaggaggcagttcaacacgcacgtaccgtgtggcagcgtcctcaccg
tcctgcaccaggactggctgaa
cgcaaggagtacaagtgcaggtctccaacaaaggcctccgtcctccatcgagaaaac
catctccaaagccaaaggcga

- 76 -

gccccgagagccacagggtgtacaccctgccccatcccaggaggatgaccaagaacca
ggtcagcctgacccgtgcctggtc
aaaggcttctaccccaagcgacatcgccgtggagtggagagcaatgggcagccggagaac
aactacaagaccacgcctccc
gtgctggactccgacggctccttcttctacagcaggctaaccgtggacaagagcagg
tggcaggagggaaatgtcttctcatgc
tccgtgatgcatgaggctctgcacaaccactacacacagaagagcctccctgtctcg
ggtaaatga.

40. A polynucleotide encoding a heterologous fusion protein of any one of Claims 1 through 389.

41. A vector comprising the polynucleotide of Claim 40.

42. A host cell comprising the vector of Claim 41.

43. A host cell expressing at least one heterologous fusion protein of any one of Claims 1 through 39.

44. The host cell of Claim 43 wherein said host cell is a CHO cell.

45. A process for producing a heterologous fusion protein comprising the steps of transcribing and translating a polynucleotide of Claim 40 under conditions wherein the heterologous fusion protein is expressed in detectable amounts.

46. A method for increasing neutrophil levels in a mammal comprising the administration of a therapeutically effective amount of the heterologous fusion protein of any one of Claims 27 through 36.

47. The use of the heterologous fusion protein as claimed in any one of Claims 22 through 29 for the manufacture of a medicament for the treatment of patients with insufficient circulating neutrophil levels.

- 77 -

48. Use of a heterologous fusion protein of any one of Claims 22 through 29 as a medicament.
49. Use of a heterologous fusion protein of any one of Claims 22 through 29 for the treatment of patients with insufficient circulating neutrophil levels.
50. A pharmaceutical formulation adapted for the treatment of patients with insufficient neutrophil levels comprising a heterologous fusion protein of any one of Claims 22 through 29.
51. A heterologous fusion protein as hereinbefore described with reference to any one of the Examples.